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Complete Specification  
entitled (54) PRODUCTION OF HIGH-PURITY RADIOACTIVE ISOTOPES.

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Related Art (56) Nil.

The following statement is a full description of this invention, including the best method of performing it known to us

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This discussion relates to the production of high purity radioactive isotopes, particularly molybdenum-99 and technetium-99m. Technetium-99m, which has a half-life of six hours, is produced by the spontaneous radioactive beta decay of molybdenum-99. The latter has a half-life of 67 hours.

High purity  $Tc^{99m}$  is used primarily as a radioisotope in medical research and diagnosis. It is well suited for liver and brain scanning, and is preferred over other radioactive isotopes because of its short half-life which results in reduced exposure of the organs to radiation.

Since the radioisotope sought to be used has such a short half-life, it is common practice to ship the users of the isotope the parent element; in this case  $Mo^{99}$ . The user then extracts the  $Tc^{99m}$  from the  $Mo^{99}$  as his needs require.

In the past, radioactive molybdenum-99 has been recovered as a fission product formed by the fissioning of uranium-235 in a nuclear reactor. This method of producing  $Mo^{99}$  has several important shortcomings. One is that the  $Mo^{99}$  has to be separated from the numerous other radioactive fission products of U-235 such as strontium-90, yttrium-91, zirconium-95, niobium-95, ruthenium-103, ruthenium-106, iodine-131, cerium-141, cesium-137, cerium-144, promethium-147 and many others. Some of these fission products are long lived, and due to their radioactivity are difficult to handle without elaborate shielding.

As a result of separation problems, pure molybdenum-99 and consequently pure  $Tc^{99m}$  cannot be obtained from U-235 fissioning because traces of fission products such as iodine-131 and ruthenium-103 frequently remain in the separated product. In addition, this technique presents radioactive waste disposal problems.

It is an object of this invention to provide a more efficient method of producing radioactive molybdenum from which radioactive technetium may be extracted. It is another object of this invention to produce radioactive molybdenum by a method which avoids the need for separating radioactive fission products and avoids problems relating to disposing of radioactive waste resulting from the fissioning of U-235. It is another object of this invention to prepare high purity technetium-99 which contains no traces of fission products.

It has now been discovered that the aforementioned objects can be achieved by a process which comprises irradiating a molybdenum containing material in the presence of a neutron flux until the desired amount of Mo<sup>99</sup> activity is formed, dissolving the irradiated material (containing Mo<sup>99</sup>) in a base, adjusting the pH of the solution to be acidic and above pH 2.5, contacting an inorganic anion exchange material with the pH adjusted solution (thereby loading the molybdenum on the anion exchange material) and then selectively eluting or extracting technetium-99m, formed by the radioactive decay of molybdenum-99, from the loaded anion exchange material with an acid.

The present method offers several advantages over prior art methods of preparing technetium-99m. One of these is elimination of the need to separate radioactive molybdenum from other radioactive fission products. Another is a considerable reduction in the radioactive waste disposal problem. A still further advantage of this invention is that a product of high purity is obtained containing no traces of other radioactive fission products. The purity of Tc<sup>99m</sup> is of considerable importance because of its medicinal use.

In order to more fully understand the invention, the following example, which is the preferred embodiment of the invention, is given by way of illustration only and is not intended to limit the scope of this invention.

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EXAMPLE

0.38 grams of  $\text{MoO}_3$  were placed in a 3/8 inch aluminum capsule and sealed. The capsule was irradiated for 75 hours in a neutron flux of  $5 \times 10^{13}$  n/cm<sup>2</sup>-sec. The resulting material containing radioactive  $\text{Mo}^{99}$  had an activity of about 135 millicuries. Following irradiation the  $\text{MoO}_3$  was dissolved in approximately 10 ml. of 40 per cent  $\text{NH}_4\text{OH}$ . The solution of ammonium molybdate,  $(\text{NH}_4)_6\text{Mo}_7\text{O}_{24} \cdot 4\text{H}_2\text{O}$  was first neutralized to a pH of 7 with 6M  $\text{HNO}_3$ , and then acidified to a pH of 3.0 to 3.5 with 1M  $\text{HNO}_3$ .

Prior to loading the above radioactive solution on an alumina anion-exchange column, the column containing 6 grams of 100 to 200 mesh alumina was washed with water and 0.1M  $\text{HNO}_3$ . Effluent from the washing step was acidic (pH 2-6) before the column was loaded. The solution of ammonium molybdate after having its pH adjusted to 3.0 to 3.5 (and which contains  $\text{Mo}^{99}$ ) was loaded on the alumina column at a flow rate of about 1-2 ml. per min. After the column was loaded, it was washed with about 150 ml. of 0.1M  $\text{HCl}$  in order to remove the small quantities of  $\text{Mo}^{99}$  that would subsequently wash through during  $\text{Tc}^{99\text{m}}$  elution and contaminate the product solution.

The loaded column which contained about 135 millicuries of activity can subsequently be eluted or milked repeatedly for  $\text{Tc}^{99\text{m}}$  as it is formed with 25 ml. portions of 0.1M  $\text{HCl}$  solution. This is done by passing the desired volume of 0.1M  $\text{HCl}$  through the column and collecting the effluent.

Numerous variations of the preferred embodiment described above may be practiced, as will be apparent to those skilled in the art, without departing from the basic concepts of the present invention. Thus, while  $\text{MoO}_3$  is the preferred target material for the production of  $\text{Mo}^{99}$ , other molybdenum containing materials may be used. Such materials include, for example, molybdenum sesquioxide,  $\text{Mo}_2\text{O}_3$ ; molybdenum dioxide,

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MoO<sub>2</sub>; molybdenum pentoxide, Mo<sub>2</sub>O<sub>5</sub>; hydrated molybdenum oxide ("moly blue"), Mo<sub>2.5-3.0</sub>·xH<sub>2</sub>O; molybdic acid H<sub>2</sub>MoO<sub>4</sub>, and mixtures thereof.

Separation of Tc<sup>99m</sup> from Mo<sup>99</sup> can be effected by contacting the Mo<sup>99</sup> (in the form of molybdate ions) with alumina, followed by selective removal of Tc<sup>99m</sup> (in the form of the TcO<sub>4</sub><sup>-</sup> ion) from the loaded alumina. A column of alumina is preferably used, however, the separation can be made by slurrying the molybdate ion containing solution with finely divided alumina in a container (thereby loading the alumina with molybdate ions), separating the solids from the liquid, for example, by filtration and then removing the Tc<sup>99</sup> from the alumina particles by reslurrying the alumina in an acid and then separating the dissolved Tc<sup>99</sup> from the unloaded alumina solids. Use of a column is, of course, far simpler and more efficient.

The exact nature of the "exchange" mechanism by which the molybdenum is loaded on alumina and by which the Tc<sup>99</sup> is eluted is not entirely certain. While not wishing to be limited to any theory, it is believed to be an ion exchange mechanism whereby molybdate ions are loaded on the acidified alumina column in exchange for OH<sup>-</sup> ions. Upon elution, the Tc<sup>99m</sup> is removed from the column as pertechnate, TcO<sub>4</sub><sup>-</sup> ions in exchange for Cl<sup>-</sup> ions. However, the ion exchange reaction appears to be limited to a surface phenomena, and it is therefore possible that the mechanism is actually a surface adsorption phenomena. It is most likely a combination of both ion exchange and adsorption. Thus, while the material is referred to in this disclosure as an inorganic "anion exchange material", it is to be understood that the materials rather than the mechanism whether ion exchange or adsorption are intended thereby. Alumina is the preferred "exchange" material.

Other materials, however, which are chemically stable in the system, stable to the radiation emitted in the system, and which are able to "exchange" the molybdenum and technetium ions can be used in place of alumina. Such materials include the inorganic refractory oxides of zirconium, thorium, tungsten and silicon. Suitable illustrative materials include zirconia ( $\text{ZrO}_2$ ), thoria ( $\text{ThO}_2$ ), tungsten trioxide ( $\text{WO}_3$ ) and silica ( $\text{SiO}_2$ ). These materials have an affinity for anions when their surfaces have been rendered acidic.

Bases other than  $\text{NH}_4\text{OH}$  may be used to dissolve the irradiated molybdenum containing material, provided they will not interfere with subsequent loading and elution of the inorganic "anion-exchange material". Suitable bases include, for example,  $\text{NaOH}$  and  $\text{KOH}$ . Ammonium hydroxide is preferred.

Following dissolution of the irradiated molybdenum containing material it is essential that the solution be acidified and be above pH 2.5. At a pH below 2.5 precipitation results, while at an alkaline pH the molybdate ion will not load properly on the "exchange" material. The preferred range is pH 3.0 to 3.5. Adjustment of the pH and washing of the "exchange" material is preferably done with  $\text{HNO}_3$ .  $\text{HCl}$  is the preferred acid used for the preferential elution of  $\text{Tc}^{99\text{m}}$  from the "exchange" material. Other mineral acids, however, such as  $\text{HNO}_3$  may also be used.

The amount of radiation to which the molybdenum containing target material is subjected is not critical and both the time and intensity of the neutron flux may be varied considerably from that shown in the preferred embodiment. It is merely necessary that the target material be irradiated until the desired amount of  $\text{Mo}^{99}$  activity is formed. A convenient amount is about 100-300 millicuries of  $\text{Mo}^{99}$  per loaded column, or about 200-1000 millicuries per gram of irradiated  $\text{MoO}_3$ .

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A process for producing radioactive technetium-99m which comprises the steps of:
  - (1) radiating a molybdenum containing material in a neutron flux until the desired amount of Mo99 activity is formed,
  - (2) dissolving the irradiated molybdenum containing material, containing the radioactive Mo99, in a base,
  - (3) adjusting the pH of the solution prepared in step (2) to be acidic and above pH 2.5,
  - (4) contacting an inorganic anion exchange material with the pH adjusted solution of step (3) thereby loading the molybdenum on the exchange material, and
  - (5) extracting technetium-99m, formed by the radioactive decay of Mo99, from the loaded anion exchange material with an acid.     - 7 JUN 1966
2. The process of claim 1 wherein the inorganic anion exchange material is alumina.     - 7 JUN 1966
3. The process of claim 2 wherein the base used to dissolve the irradiated material is ammonium hydroxide.     - 7 JUN 1966
4. The process of claim 2 wherein the pH of the solution prepared in step (2) is adjusted to be within the range of 3.0 to 3.5.     - 7 JUN 1966
5. The process of claim 2 wherein the particle size of the alumina is 100 to 200 mesh.     - 7 JUN 1966
6. The process of claim 2 wherein the acid used for extracting the technetium-99m from the loaded alumina is hydrochloric acid.     - 7 JUN 1966

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7. A process for producing radioactive technetium-99m which comprises the steps of:

- (1) radiating  $\text{MoO}_3$  in a neutron flux until the desired amount of  $\text{Mo}^{99}$  activity is formed,
- (2) dissolving the irradiated  $\text{MoO}_3$ , containing radioactive  $\text{Mo}^{99}$ , in ammonium hydroxide,
- (3) adjusting the pH of the solution formed in step (2) to be acidic and above pH 2.5,
- (4) contacting a column of alumina with the pH adjusted solution of step (3) thereby loading the alumina with molybdate ions, and
- (5) eluting technetium-99m, formed by the radioactive decay of  $\text{Mo}^{99}$ , from the loaded alumina column with hydrochloric acid.

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8. The process of claim 7 wherein the pH of the solution formed in step (2) is adjusted to be within the range of 3.0 to 3.5.

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9. A process for producing radioactive technetium-99m which comprises the steps of:

- (1) providing a solution of ammonium molybdate,
- (2) adjusting the pH of the solution to be acidic and above pH 2.5,
- (3) contacting a column of alumina with the pH adjusted solution of step (2), thereby loading the column with molybdate ions, and
- (4) eluting technetium-99m, formed by the radioactive decay of  $\text{Mo}^{99}$ , from the loaded alumina column with an acid.

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10. The process of claim 9 wherein the pH of the solution is adjusted to be within the range of 3.0 to 3.5.

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11. The process of claim 9 wherein the acid used for eluting the loaded alumina column is hydrochloric acid.

12. A process for producing radioactive technetium-99m which comprises the steps of:

(1) providing a solution containing molybdate ions, which is acidic and has a pH above 2.5,

(2) loading a column of alumina with the solution of step (1), and

(3) eluting technetium-99m, formed by the radioactive decay of Mo<sup>99</sup>, from the loaded alumina column with an acid.

13. The process of claim 12 wherein the pH of the solution is adjusted to be within the range of 3.0 to 3.5.

14. The process of claim 12 wherein the acid used for eluting the loaded alumina column is hydrochloric acid.

15. A process for producing radioactive molybdenum-99 which comprises the steps of:

(1) radiating MoO<sub>3</sub> in a neutron flux until the desired amount of Mo<sup>99</sup> activity is formed,

(2) dissolving the irradiated MoO<sub>3</sub>, containing radioactive Mo<sup>99</sup>, in a base, and

(3) adjusting the pH of the solution formed in step (2) to be acidic and above pH 2.5.

16. A process for producing radioactive molybdenum-99 which comprises the steps of:

(1) irradiating MoO<sub>3</sub> in a neutron flux until the desired amount of Mo<sup>99</sup> activity is formed,

(2) dissolving the irradiated MoO<sub>3</sub>, containing radioactive Mo<sup>99</sup>, in ammonium hydroxide and,

(3) adjusting the pH of the solution prepared in step (2) to be within the range of 3.0 to 3.5. -7 JUN 1966

17. A process for producing radioactive molybdenum-99 which comprises the steps of:

- (1) radiating  $\text{MoO}_3$ , in a neutron flux until the desired amount of  $\text{Mo}^{99}$  activity is formed,
- (2) dissolving the irradiated  $\text{MoO}_3$ , containing radioactive  $\text{Mo}^{99}$ , in a base,
- (3) adjusting the pH of the solution formed in step (2) to be acidic and above pH 2.5, and
- (4) loading the pH adjusted solution of step (3) on a column of alumina. -7 JUN 1966

18. A process for producing radioactive molybdenum-99 which comprises the steps of:

- (1) radiating  $\text{MoO}_3$  in a neutron flux until the desired amount of  $\text{Mo}^{99}$  activity is formed,
- (2) dissolving the irradiated  $\text{MoO}_3$  containing radioactive  $\text{Mo}^{99}$  in ammonium hydroxide,
- (3) adjusting the pH of the solution prepared in step (2) to be within the range of 3.0 to 3.5, and
- (4) loading the pH adjusted solution of step (3) on a column of alumina. -7 JUN 1966

19. Irradiated  $\text{MoO}_3$  containing radioactive  $\text{Mo}^{99}$ . -7 JUN 1966

20. Irradiated  $\text{MoO}_3$  containing radioactive  $\text{Mo}^{99}$  and having an activity of about 200-1000 millicuries per gram of  $\text{MoO}_3$ . -7 JUN 1966

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21. A process for producing radioactive technetium -99m substantially as described with reference to the example. JUN 1966

22. A process for producing radioactive molybdenum-99 substantially as described with reference to the example. JUN 1966

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